

### AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A method for the separation and purification of fibrinogen and plasminogen which comprises the steps of:

(a) loading a solution comprising fibrinogen and plasminogen onto an immobilized metal ion affinity chromatography matrix under conditions such that the fibrinogen and the plasminogen both bind to the matrix, and

(b) selectively eluting the fibrinogen and the plasminogen separately from the matrix,

wherein the immobilized metal ion affinity chromatography matrix is a copper, nickel or zinc ion affinity chromatography matrix;

wherein plasminogen is eluted using a buffer comprising a low concentration of a low molecular weight competitive chelating compound, a reduced pH compared to the loading solution, or a reduced ionic strength compared to the loading solution, wherein fibrinogen remains bound;

wherein fibrinogen is eluted using a buffer comprising a higher concentration of the same or a different low molecular weight competitive chelating compound, a reduced pH compared to the loading solution or the buffer used to elute plasminogen, or a reduced ionic strength compared to the loading solution or the buffer used to elute plasminogen;  
and

wherein the competitive chelating compound is selected from the group consisting of an amino acid, imidazole, EDTA and a citrate salt.

2. **(Canceled)**

3. **(Currently amended)** A method for the separation of fibrinogen from plasminogen comprising the steps of:

(a) loading a solution comprising fibrinogen and plasminogen onto an immobilized metal ion affinity chromatography matrix under conditions such that at least the fibrinogen binds to the matrix, and

(b) selectively eluting the fibrinogen from the matrix,

wherein the immobilized metal ion affinity chromatography matrix is a copper, nickel or zinc ion affinity chromatography matrix;

wherein the fibrinogen is eluted using a buffer comprising more than 20 mM of a competitive chelating compound, a reduced pH compared to the loading solution, or a reduced ionic strength compared to the loading solution;

wherein the competitive chelating compound is selected from the group consisting of an amino acid, imidazole, EDTA and a citrate salt.

4. **(Currently amended)** The method according to claim 3, wherein the plasminogen and the fibrinogen are selectively eluted separately from the matrix,

wherein plasminogen is eluted using a buffer comprising  $\leq 20$  mM of a competitive chelating compound, a reduced pH compared to the loading solution, or a reduced ionic strength compared to the loading solution;

wherein the competitive chelating compound is selected from the group consisting of an amino acid, imidazole, EDTA and a citrate salt.

5. **(Previously presented)** The method according to claim 1 or 3, wherein the solution comprising fibrinogen is a fibrinogen-containing plasma fraction.

6.-15. **(Canceled)**

16. **(Withdrawn- Currently amended)** A lyophilized fibrinogen formulation comprising fibrinogen of Claim 11, factor XIII, a carbohydrate, an amino acid, a salt, a buffer and a detergent, the formulation being capable of dissolution in water at ambient temperature in less than 15 minutes to give a fibrinogen solution.

17. **(Withdrawn)** The formulation according to claim 16, wherein the concentration of the fibrinogen solution is at least about 60 mg/ml.

18. **(Withdrawn)** The formulation according to claim 16, which is heat treated to inactivate viruses.

19. **(Withdrawn)** The formulation according to claim 16, which is free from anti-fibrinolytic agents.

20. **(Withdrawn)** The formulation according to claim 16, which is free from stabilizing proteins such as albumin.

21. **(Canceled)**

22. **(Withdrawn)** The lyophilized fibrinogen formulation of Claim 16, wherein the formulation being capable of dissolution in water at ambient temperature in less than 10 minutes to give a fibrinogen solution.

23. **(Withdrawn)** The lyophilized fibrinogen formulation of Claim 16, wherein the formulation being capable of dissolution in water at ambient temperature in less than 5 minutes to give a fibrinogen solution.

24. **(Previously presented)** The method of Claim 1 or 3 further comprising the step of concentrating the fibrinogen by ultrafiltration to a concentration of approximately 15 to 30 mg/ml.

25. **(Previously presented)** The method of Claim 24 further comprising the steps of:  
combining the fibrinogen with a combination of suitable stabilizers to form a fibrinogen formulation;  
sterilizing the fibrinogen formulation by filtration; and  
lyophilizing the fibrinogen formulation to form a lyophilized fibrinogen formulation.

26. **(Previously presented)** The method of Claim 25, wherein the stabilizers are selected from the group consisting of an amino acid, a carbohydrate, a salt, and a detergent.

27. **(Previously presented)** The method of Claim 25 further comprising the step of subjecting the lyophilized fibrinogen formulation to dry heat treatment.

28. **(New)** The method of Claim 1, wherein plasminogen is eluted using a buffer comprising  $\leq 20$  mM of a low molecular weight competitive chelating compound and wherein fibrinogen is eluted using a buffer comprising  $> 20$  mM of the same or a different competitive chelating compound.

29. **(New)** The method of Claim 1 or 3, wherein the competitive chelating compound used to elute plasminogen is an amino acid selected from the group consisting of alanine, leucine and lysine, and the competitive chelating compound used to elute fibrinogen is an amino acid selected from the group consisting of lysine and arginine.

30. **(New)** The method of Claim 29, wherein the competitive chelating compound used to elute plasminogen is selected from the group consisting of  $\leq 20$  mM alanine,  $\leq 20$  mM leucine and  $\leq 10$  mM lysine.

31. (New) The method of Claim 1, wherein fibrinogen is eluted using a buffer comprising more than 20 mM of lysine, arginine or imidazole.

32. (New) The method of Claim 1 or 3, wherein the buffers for eluting plasminogen and/or fibrinogen comprise a salt of citrate, phosphate and/or chloride.

33. (New) The method of Claim 1 or 3, wherein the buffers for eluting plasminogen and/or fibrinogen have a pH in the range of 6-8.

34. (New) The method of Claim 1 or 3, wherein the buffer for eluting plasminogen comprises 20 mM phosphate, 15 mM alanine and 0.5 M chloride and the buffer for eluting fibrinogen comprises 10 mM citrate, 50 mM arginine and 50 mM chloride.